Amendments to the Specification

Please replace the Brief Description of the Drawings section, beginning on page 12 of the specification, with the following amended Brief Description of the Drawings section:

Brief Description of the Drawings

Figure 1 is a partial schematic diagram of a Ras pathway.

Figure 2A shows human (h) and mouse (m) CalDAG-GEFI, human (h) and rat (r) CalDAG-GEFII, and *C. elegans* (cel) (F25B3.3, GenBank accession number: 1262950) CalDAG-GEF.

_____Figure 2B shows a computer-generated phylogenetic tree analysis of the GEF domains of hCalDAG-GEFI and hCalDAG-GEFII in relation to mCdc25, hSos1, C3G , rRas-GRF, *C. elegans* (cel) (F25B3.3, GenBank accession number: 1262950) and BUD5other Ras superfamily GEFs.

_____Figure 2C shows multiple alignment of GEF structurally conserved regions (SCRs) of F25B3.3 (SEQ. ID NOS. 19, 20 and 21), hCalDAG-GEFI (SEQ. ID NO: 4: 150–173, 219-262 and 298-320), hCalDAG-GEFII (SEQ. ID NO: 8: 205-229, 270-313, and 348-371), C3G (SEQ. ID NOS. 22, 23 and 24), mCdc25 (SEQ. ID NOS. 25, 26 and 27), rRas-GRF (SEQ. ID NOS. 28, 29 and 30), hSos1 (SEQ. ID NOS. 31, 32 and 33), BUD5 (SEQ. ID NOS. 34, 35 and 36) and *C. elegans* (cel) (F25B3.3, GenBank accession number: 1262950)(SEQ.ID NO: 37).s and several other GEFs of the Ras superfamily.

_____Figure 2D shows the full-length amino acid sequences of human (h) (SEQ. ID NO: 4), and mouse (m) (SEQ. ID NO: 2) CalDAG-GEFI (box indicates amino acid differences).

_____Figure 2E shows the sequence similarity (black indicates identity) of EF-hand domains in hCalDAG-GEFI (SEQ. ID NO: 4: 432-452), hCalDAG-GEFII (SEQ. ID NO: 8: 427-447), hCalmodulin (SEQ. ID NO: 38), hCalbindin D28K (SEQ. ID NO: 39), hCalcineurin B (SEQ. ID NO: 40), hParvalbumin α (SEQ. ID NO: 41), hTroponin C (SEQ. ID NO: 42), and *C. elegans* (cel)(F25B3.3, GenBank accession number: 1262950 (SEQ. ID NO: 37)s and other calcium binding proteins.

_____Figure 2F shows the sequence similarity of DAG-binding domains of hCalDAG-GEFI (SEQ. ID NO: 4: 498-548), hCalDAG-GEFII (SEQ. ID NO: 8: 492-542), hPKCα (SEQ. ID NO: 44), hPKCβ1 (SEQ. ID NO: 45), hPKCγ (SEQ. ID NO: 46) and _C. elegans_ (cel) (F25B3.3, GenBank accession number: 1262950)(SEQ. ID NO: 43)s and PKC (protein kinase C) family proteins.

Figure 3A is a schematic representation of human (h) cAMP-GEFI family protein.s, including human (h) and rat (r) cAMP GEFI, human (h) cAMP GEFII and _C. elegans_ (cel) (T20G5.5, GenBank accession number: 458480) cAMP GEF. ___

_____Figure 3B is a phylogenetic tree analysis of cAMP binding domains of cAMP-GEFI and II and other cyclic nucleotide binding proteins.

_____Figure 3C is a phylogenetic tree analysis of GEF domains of cAMP-GEFI and II and other Ras superfamily GEFs.

_____Figure 3D shows the amino acid sequences of the structurally conserved regions (SCRs) of cAMP GEFs human (h) cAMP-GEFI (SEQ. ID NO: 12: 616-639, 688-731 and 767-789), rat (r) cAMP-GEFI (SEQ. ID NO: 10: 618-642, 691-734 and 770-792), human (h) cAMP-GEFII (SEQ. ID NOS. 48 and 18: 767-791, 839-882 and 918-940), rat (r) cAMP-GEFII (SEQ. ID NO: 16: 192-216, 264-307 and 343-365), celcAMP-GEF (SEQ. ID NO: 47, 49 and 50), hCalDEG-GEFI (SEQ. ID NO: 4: 150-173, 219-262 and 298-320), hCalDAG-GEFII (SEQ. ID NO: 8: 205-229, 270-313, and 348-371), C3G (SEQ. ID NOS. 22, 23 and 24), CDC25 (SEQ. ID NOS. 25, 26 and 27), rRas-GRF (SEQ. ID NOS. 28, 29 and 30), hSos1 (SEQ. ID NOS. 31, 32 and 33), and BUD5 (SEQ. ID NOS. 34, 35 and 36).and other Ras superfamily GEFs (black indicates identity).

_____Figure 3E shows the amino acid sequences of the cAMP binding pockets of human (h) cAMP-GEFI (SEQ. ID NO: 12), and rat (r) cAMP-GEFI (SEQ. ID NO: 10), human (h) cAMP-GEFII (SEQ. ID NO: 18), celcAMP-GEF (SEQ. ID NO: 51), hPKARIa A (SEQ. ID NO: 52), hPKARIIa A (SEQ. ID NO: 53), hPKARIa B (SEQ. ID NO: 54), hPKARIIa B (SEQ. ID NO: 55), hPKGIa (SEQ. ID NO: 56), hPKGIb (SEQ. ID NO: 57), and hPKGII (SEQ. ID NO: 58). cAMP GEFI and II and other cyclic nucleotide binding proteins. The positions of invariant amino acid residues are shown by black diamonds. The open diamond indicates the amino acid that

determines the binding specificity for cAMP or cGMP. The arrow indicates the position of amino acid substitutions specific to cAMP-GEFs.

_____Figure 3F is the full-length amino acid sequences of human cAMP-GEFI (SEQ. ID NO: 12) and human cAMP-GEFII (SEQ. ID NO: 18)(boxes indicate amino acid identity).

On page 16 of the specification, line 1, please replace SEQ ID NO: 18 with SEQ ID NO: 17.

On page 16 of the specification, line 2, please replace SEQ ID NO: 19 with SEQ ID NO: 18.

On page 22, TABLE I, please replace the row beginning with hcAMP-GEFI with the following amended row:

| hcAMP-GEFI | SEQ ID NO.11:
2058-2130
SEQ ID NO.12:
~~205-229~~616-639 | SEQ ID NO.11:
2276-2405
SEQ ID NO.12:
688-731 | SEQ ID NO.11:
2516-2582
SEQ ID NO.12:
767-789 |